**Citation:**

Rankin JW, Turpyn AD. Low carbohydrate, high fat diet increases C-reactive protein during weight loss. *J Am Coll Nutr*. 2007 Apr;26(2):163-9.

**PubMed ID:** 17536128

**Study Design:**

Randomized Controlled Trial

**Class:**

A - Click here for explanation of classification scheme.

**Research Design and Implementation Rating:**

POSITIVE: See Research Design and Implementation Criteria Checklist below.

**Research Purpose:**

To determine the effect of weight loss diet composition (low CHO, high fat or high CHO low fat) on inflammation and if this was related to oxidative stress.

**Inclusion Criteria:**

Female, pre-menopausal, weight stable for ≥ 6 months, nonsmokers, BMI > 24.5, sedentary (< 5 hours of exercise/week), otherwise healthy.

**Exclusion Criteria:**

Contraindications for weight loss, diabetes, CVD, HTN, rheumatoid arthritis, Crohn's disease, lupus, medications known to influence inflammation.

**Description of Study Protocol:**

**Recruitment** from a local community and screened for study criteria.

**Design:** Randomized controlled trial

- Random assignment to one of two weight loss diets: ad libitum low CHO, high fat, high protein (LC) or calorie restricted high CHO, low fat, low protein (HC).
- Diet followed for 4 weeks with LC group provided with Atkin's book and handouts and HC group provided with exchange system plan based on body weight.
- Energy goals for HC group were determined by estimated RMR for .5 - 1.0 lb/week loss.
- Weekly 4 day food records were kept by subjects for compliance measures. Each week urine and blood was collected, weight was measured, and waist and hip circumferences were measured.

**Blinding used (if applicable)** not mentioned

**Intervention (if applicable)** 4 week weight loss diets as described above with weekly education and social support.

**Statistical Analysis**

- Baseline characteristics compared across groups by t-test.
- Mixed model repeated measures ANOVA used to analyze dependent measures with weekly values.
- Differences among means from the groups were analyzed using Tukey's LSD test.
- Changes in dependent measures from baseline to week 4 were analyzed by t-test.
- Associations between dependent measures analyzed by Pearson Product moment correlation.
- p value < .05 used for significance.

**Data Collection Summary:**

**Timing of Measurements** at baseline and weekly for duration of study (4 weeks).

**Dependent Variables**

- Body weight on a calibrated scale
- Waist and hip circumferences measured
- C-reactive protein (CRP)
- IL-6
- 8-Epi (pg/mg creatinine) from urine
- FBG
- Non-esterified fatty acids (NEFA)

**Independent Variables**

- Ad lib low CHO, high fat, high protein diet (LC)
- Calorie restricted high CHO, low fat, low protein diet (HC) with goals of 15-20% of kcals as protein, 20-25% fat and 60% CHO

**Control Variables**

- Age

**Description of Actual Data Sample:**

**Initial N**: 32 females

**Attrition (final N):** 29 (3 discontinued the study by choice)

**Age**: 32 - 45 yo; LC group = 38.8 $\pm$ 3.8 yrs (mean $\pm$ SD); HC group = 40.1 $\pm$ 3.0 yrs

**Ethnicity**: 28 Caucasian, 2 African American, 2 Asian, 1 Indian

**Other relevant demographics**:

**Anthropometrics**

- All subject BMI at baseline: 32.1 ± 5.4; Baseline BMI for LC group 32.7 ±5.5, HC group 31.4 ± 5.4
- Weight at baseline by group: LC = 87.3 ± 15.2 kg, HC 79.2 ± 16.0 kg
- Weight: height ratio at baseline by group: LC 0.78 ± 0.06, HC 0.81 ± 0.05
- No differences between groups at baseline

**Location**: local community to Blacksburg, VA

**Summary of Results:**

**Key Findings:**

- All subjects lost a significant amount of weight and the LC group lost more than the HC group ($p<0.05$) especially during the first week.
- Vitamin A intake was higher for the HC than the LC during the weight loss period.
- Serum glucose decreased over the 4 weeks but there was no difference between groups in serum glucose at baseline or week 4.
- Reduction in BG was negatively correlated with the change in serum non-esterified fatty acids (NEFA) ($r = -0.55$, $p=0.002$).
- Serum IL-6 increased for both groups but there was no difference between groups.
- There was a significant interaction of groups over time for serum CRP with CRP increasing for the LC group and decreasing for the HC group by week 4 (+25% vs. -43%, $p = 0.02$).
- There was no consistent effect of wt loss on 8-Epi excretion.
- Study did not support a link between macronutrient composition of the diets and oxidative stress.

| Measure | Group | Baseline | Week 4 | Difference from Baseline |
|---|---|---|---|---|
| Weight (kg) | LC | 87.3 ± 15.0 | 83.5 ± 14.8 | P<0.01 |
| | HC | 79.2 ± 16.0 | 76.6 ± 15.7 | P<0.01 |
| CRP (mg/L) | LC | 5.7 ± 5.5 | 7.1 ± 6.1 | P<0.05 |
| | HC | 4.8 ± 4.2 | 2.7 ± 2.9 | P<0.01; different from LC p<0.05 |
| IL-6 (pg/mL) | LC | 1.60 ± 0.78 | 1.78 ± 0.73 | |
| | HC | 1.20 ± 0.76 | 1.47 ± 1.03 | |
| 8-Epi (pg/mg creatinine) | LC | 1576 ± 511 | 1495 ± 797 | |
| | HC | 1246 ± 543 | 1064 ± 624 | |
| Glucose (mg/dl) | LC | 85.6 ± 5.5 | 81.6 ± 7.5 | p< 0.01 for both groups together |
| | HC | 84.7 ± 10.7 | 83.3 ± 4.7 | |
| NEFA (mEq/L) | LC | 0.32 ± 0.13 | 0.56 ± 0.24 | |
| | HC | 0.27 ± 0.10 | 0.36 ± 0.14 | |

**Other Findings**

- Dietary intake between groups at baseline was not different. Reported caloric intake between groups was similar during the wt loss period.
- The percent of kcalories from fat, CHO, and protein was significantly different between

groups for all four weeks of the diet, $p < 0.01$.
- Vitamin A intake was greater for the HC group during all 4 weeks of the diet, $p< 0.01$ at weeks 1,2, and 3; $p< 0.05$ at week 4.
- Vitamin C intake for the HC group was twice that of the LC group during all 4 weeks of the diet yet no p values are given.

**Author Conclusion:**

Diet composition influenced serum C-reactive protein as a marker of inflammation in that the LC increased it while the HC decreased it however this was not related to measures of oxidative stress.

***Reviewer Comments:***

*Dietary compliance was monitored by 4 day food records each week.*

*Limitations of the study include blinding was not mentioned, diets varied in protein in addition to fat and CHO, 8-Epi may not have been a sensitive enough marker to measure oxidative stress, variability among subjects in compliance, and short study period.*

*Did not specify which groups the 3 drop outs were from however they quit the study within the first week and data was not used.*

*Exercise was not monitored though the subjects were "sedentary".*

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***Research Design and Implementation Criteria Checklist: Primary Research***

| **Relevance Questions** | | |
|---|---|---|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

| **Validity Questions** | | |
|---|---|---|
| **1.** | **Was the research question clearly stated?** | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |

| | | |
|---|---|---|
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| **2.** | **Was the selection of study subjects/patients free from bias?** | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | Yes |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |
| 2.4. | Were the subjects/patients a representative sample of the relevant population? | ??? |
| **3.** | **Were study groups comparable?** | Yes |
| 3.1. | Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) | Yes |
| 3.2. | Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? | Yes |
| 3.3. | Were concurrent controls used? (Concurrent preferred over historical controls.) | No |
| 3.4. | If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis? | N/A |
| 3.5. | If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.) | N/A |
| 3.6. | If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")? | N/A |
| **4.** | **Was method of handling withdrawals described?** | Yes |
| 4.1. | Were follow-up methods described and the same for all groups? | Yes |
| 4.2. | Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.) | No |
| 4.3. | Were all enrolled subjects/patients (in the original sample) accounted for? | Yes |
| 4.4. | Were reasons for withdrawals similar across groups? | ??? |

| | | |
|---|---|---|
| 4.5. | If diagnostic test, was decision to perform reference test not dependent on results of test under study? | N/A |
| **5.** | **Was blinding used to prevent introduction of bias?** | Yes |
| 5.1. | In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate? | ??? |
| 5.2. | Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.) | Yes |
| 5.3. | In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded? | N/A |
| 5.4. | In case control study, was case definition explicit and case ascertainment not influenced by exposure status? | N/A |
| 5.5. | In diagnostic study, were test results blinded to patient history and other test results? | N/A |
| **6.** | **Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?** | Yes |
| 6.1. | In RCT or other intervention trial, were protocols described for all regimens studied? | Yes |
| 6.2. | In observational study, were interventions, study settings, and clinicians/provider described? | N/A |
| 6.3. | Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect? | Yes |
| 6.4. | Was the amount of exposure and, if relevant, subject/patient compliance measured? | Yes |
| 6.5. | Were co-interventions (e.g., ancillary treatments, other therapies) described? | N/A |
| 6.6. | Were extra or unplanned treatments described? | N/A |
| 6.7. | Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups? | Yes |
| 6.8. | In diagnostic study, were details of test administration and replication sufficient? | N/A |
| **7.** | **Were outcomes clearly defined and the measurements valid and reliable?** | Yes |
| 7.1. | Were primary and secondary endpoints described and relevant to the question? | Yes |
| 7.2. | Were nutrition measures appropriate to question and outcomes of concern? | Yes |
| 7.3. | Was the period of follow-up long enough for important outcome(s) to occur? | Yes |
| 7.4. | Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures? | Yes |

| | | | |
|---|---|---|---|
| | 7.5. | Was the measurement of effect at an appropriate level of precision? | Yes |
| | 7.6. | Were other factors accounted for (measured) that could affect outcomes? | ??? |
| | 7.7. | Were the measurements conducted consistently across groups? | Yes |
| **8.** | **Was the statistical analysis appropriate for the study design and type of outcome indicators?** | | Yes |
| | 8.1. | Were statistical analyses adequately described and the results reported appropriately? | Yes |
| | 8.2. | Were correct statistical tests used and assumptions of test not violated? | Yes |
| | 8.3. | Were statistics reported with levels of significance and/or confidence intervals? | Yes |
| | 8.4. | Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)? | N/A |
| | 8.5. | Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)? | No |
| | 8.6. | Was clinical significance as well as statistical significance reported? | Yes |
| | 8.7. | If negative findings, was a power calculation reported to address type 2 error? | No |
| **9.** | **Are conclusions supported by results with biases and limitations taken into consideration?** | | Yes |
| | 9.1. | Is there a discussion of findings? | Yes |
| | 9.2. | Are biases and study limitations identified and discussed? | Yes |
| **10.** | **Is bias due to study's funding or sponsorship unlikely?** | | Yes |
| | 10.1. | Were sources of funding and investigators' affiliations described? | Yes |
| | 10.2. | Was the study free from apparent conflict of interest? | Yes |